NOT FOR PUBLICATION

UNITED STATES DISTRICT COURT
DISTRICT OF NEW JERSEY

GLAXO GROUP LIMITED, and SMITHKLINE BEECHAM CORPORATION,	:	Civil Action No. 03-CV-399 (JLL)
Plaintiffs,	:	
v.	:	OPINION
KALI LABORATORIES, INCORPORATED,	:	
Defendant.	:	LINARES, District Judge

INTRODUCTION

This matter is before the Court on defendant's motions for a claim construction, for summary judgment that plaintiffs are not entitled to their foreign priority date, and for summary judgment of invalidity on the basis of plaintiffs' inequitable conduct; and on plaintiffs' motions for summary judgment that the priority document complies with the written description and enablement requirements of 35 U.S.C. § 112, for summary judgment of no inequitable conduct, and for summary judgment of infringement. The Court has considered the submissions in support of and in opposition to these motions, as well as the oral arguments advanced by the parties on July 11, 2005.

BACKGROUND

This action concerns plaintiffs' patented drug ondansetron, sold under the tradename Zofran®, which combats nausea and vomiting. Defendant filed an Abbreviated New Drug Application (ANDA) on September 30, 2002, seeking to sell a generic version of Zofran®. This action for patent infringement ensued.

The patents-in-suit are the so-called "Tyers" patents: TYERS I and II. TYERS I claims, in relevant part[1]:

> 1. A method of treatment for the relief of nausea and vomiting which comprises administering to a human or animal subject in need thereof an effective amount for treatment for the relief of nausea and vomiting of [ondansetron] or a physiologically acceptable salt or solvate thereof.

U.S. Patent No. 4,753,789, claim 1 (issued June 28, 1988) [hereinafter "'789 patent" or "TYERS I"]. TYERS II claims, in relevant part:

> 1. A method of treatment of nausea and vomiting which comprises administering to a human or animal subject in need thereof an effective amount for the treatment of nausea and vomiting of [ondansetron].

U.S. Patent No. 5,578,628, claim 1 (issued Nov. 26, 1996) [hereinafter "'628 patent" or "TYERS II"].

On June 25, 1985, plaintiff Glaxo Group Limited ("Glaxo") filed a patent application in the United Kingdom for ondansetron and related compounds. (See Request for a Grant of Patent of 6/25/85 ("UK Application").) That application described the invention as relating "to certain tetrahydrocarbazolone derivatives which may be used to promote gastric emptying and as anti-

[1]Plaintiffs allege infringement of claims 1, 4, 6, 8, 10, 12, 13, and 16 of TYERS I, and claims 1 and 2 of TYERS II. The first claims of both patents, however, being both independent and the broadest, are the subject of the Court's analysis in these motions.

emetics." (UK Application at 1.) It further claimed that "[r]esults from patients suffering from the symptoms of nausea indicate that [ondansetron] alleviate[s] the symptoms of nausea." (Id. at 6.) The basis for this assertion, at least in part, was an uncontrolled pilot study of ondansetron's effect on migraine, which was conducted at a West German clinic. The West German study revealed no appreciable migraine relief, but it did demonstrate relief of nausea in certain patients. (See Glaxo Group Research Ltd., A Pilot Study to Evaluate GR38032 in the Treatment of Migraine, Aug. 1985, at 2.)

On June 24, 1986, Glaxo filed with the U.S. Patent and Trademark Office ("PTO") an application for these compounds, claiming priority to the UK application. TYERS I issued from this application on June 28, 1988.

On March 30, 1990, Glaxo filed another U.S. application for the compounds, again claiming priority to the UK application. While Glaxo was prosecuting this patent (i.e., TYERS II), an Interference was declared between TYERS II and the so-called Wootton patent, which was owned by Beecham Corporation. Glaxo prevailed and TYERS II eventually issued on November 26, 1996.

Plaintiffs and defendant have moved for summary judgment on various grounds, which are discussed fully below.

DISCUSSION

I. *Summary Judgment Standard*

A party is entitled to summary judgment when it demonstrates that there is no genuine issue of material fact and that the evidence establishes its entitlement to judgment as a matter of

law. Fed. R. Civ. P. 56(c); Celotex Corp. v. Catrett, 477 U.S. 317, 322-23 (1986); Orson, Inc. v. Mirimax Film Corp., 79 F.3d 1358, 1366 (3d Cir. 1996). Put another way, summary judgment will be granted when the evidence on the record "is so one-sided that one party must prevail as a matter of law." Anderson v. Liberty Lobby, Inc., 477 U.S. 242, 251-52 (1986).

The movant carries the initial burden of supporting its motion, but once the movant has satisfied this burden, the opposing party must then "produce specific facts" sufficient to "create a fair doubt" over whether the movant should prevail. Jersey Cent. Power & Light Co. v. Lacey Township, 772 F.2d 1103, 1109 (3d Cir. 1985). The non-moving party cannot rest on mere allegations and must instead present actual evidence that creates a genuine issue as to a material fact for trial. Fed. R. Civ. P. 56(e); Siegel Transfer, Inc. v. Carrier Express, Inc., 54 F.3d 1125, 1130-31 (3d Cir. 1995). In considering a motion for summary judgment, the Court views all evidence in a light most favorable to the party opposing the motion. Brewer v. Quaker State Oil Ref. Corp., 72 F.3d 326, 330 (3d Cir. 1995).

II. *Claim Construction*

Preliminarily, the Court addresses a claim construction dispute that has arisen in the context of these motions. Both parties agree that the Court should neither add nor disregard language in claim 1 of both TYERS I and II – the broadest of the claims at issue – but defendant argues, in essence, that these claims should be read as limitless, encompassing all nausea induced by whichever source and mediated by whichever pathway. Plaintiffs counter that no skilled artisan would read the claims as such.

Again, the relevant claims are as follows:

A method of treatment for the relief of nausea and vomiting which comprises

> administering to a human or animal subject in need thereof an effective amount for treatment for the relief of nausea and vomiting of [ondansetron] or a physiologically acceptable salt or solvate thereof[; and]
>
> A method of treatment of nausea and vomiting which comprises administering to a human or animal subject in need thereof an effective amount for the treatment of nausea and vomiting of [ondansetron].

'789 patent, claim 1; '628 patent, claim 1.

The Court accords the claim terms their plain and ordinary meaning, as understood by those skilled in the art, and presumes that these "mean what they say." Texas Digital Sys., Inc. v. Telegenix, Inc., 308 F.3d 1193, 1202 (Fed. Cir. 2002). Consequently, as the plain language of these claims places no limitation on the types of nausea combated by ondansetron, and plaintiffs concede that these claims apply to any effective administration of ondansetron so long as the subject is suffering (or will suffer) from nausea (see Tr. of Proceedings of 7/11/05, at 32, 40-42), the Court will not read any such limitation into the claims.

By the same token, however, the Court does not construe these claims to create a panacea, as it were, for the general condition of nausea and vomiting. To do so would be to interpret the claims in a manner no person skilled in the art would deem tenable. TYERS I and II claim "a method of treatment" whereby ondansetron is administered in "an effective amount" to relieve nausea and vomiting. '789 patent, claim 1; '628 patent, claim 1. By their terms, therefore, the claims are directed to a successful course of treatment for relieving nausea with certain dosages of a certain compound. See Kao Corp. v. Unilever United States, Inc., 334 F. Supp. 2d 527, 546 (D. Del. 2004) (construing "amount effective" to mean, in part, conferring a "benefit"). That compound, ondansetron, is described in the patent's specification as a "potent and selective antagonist[]" of the 5-HT_3 receptor. '789 patent, col. 2:5-10. Thus, in light of the context of the

patents' claim language, as further illuminated by the specification, the Court will not construe TYERS I and II as claiming a cure-all for all human and animal forms of nausea, as no skilled artisan would interpret these as such.[2] See Medrad, Inc. v. MRI Devices Corp., 401 F.3d 1313, 1319 (Fed. Cir. 2005) (rejecting litigant's attempt to interpret claims without context of how the invention works as described in the specification); V-Formation, Inc. v. Benetton Group SpA, 401 F.3d 1307, 1311 (Fed. Cir. 2005) (stating that the specification is usually the best source for discerning claim context as understood by those skilled in the art).

In sum, the Court holds that the relevant claim language – namely, "a method of treatment for the relief of nausea and vomiting which comprises administering to a human or animal subject in need thereof an effective amount for treatment for the relief of nausea and vomiting of [ondansetron]" – means what it says. The claims reach administration of ondansetron for the treatment of nausea, however induced, but only those manifestations of nausea against which ondansetron, a 5-HT_3 antagonist, is effective. Put another way, TYERS I and II are directed to any use of ondansetron that may work to treat a patient's nausea, but these patents do not claim a method of treatment for the relief of those forms of nausea, such as apomorphine-induced nausea, against which it would be obvious to skilled artisans that a 5-HT_3 antagonist is ineffective.

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[2]Indeed, defendant's own experts testified, in essence, that they interpret – or that a skilled artisan in 1985 would have interpreted – these claims as directed only to those forms of nausea potentially mediated by the 5-HT_3 receptor. (See Hain Dep. at 213:18-214:14; Davis Dep. at 217:22-219:12.) Dr. Davis in particular stated: "If I take myself back to [1985] and I was apprised of this information, my prediction if it was potent and selective up to 5-HTM, that, by definition, it would not also be active at the D2 receptors." (Davis Dep. at 219:4-8 (emphasis added).)

III. *Enablement*

Both parties have moved for summary judgment concerning the issue of enablement under 35 U.S.C. §§ 112, 119. Plaintiffs contend that the UK application furnishes sufficient guidance to those skilled in the art to practice the invention claimed in TYERS I and II, and that no reasonable fact-finder could find otherwise, as evidenced by the PTO's and the District of Delaware's findings of enablement involving the same documents. Defendant argues that the UK application merely "hypothesizes" that ondansetron could be an effective anti-emetic, that the art was and still is highly unpredictable, and that the data upon which it was based, namely, the West German studies, were meaningless. For these reasons among others, defendant maintains that the UK application does not enable the TYERS claims.

To be accorded priority over a competing application pursuant to 35 U.S.C. § 119, a foreign application must comply with the specification requirements of § 112; that is, it must "enable" one skilled in the art to use the invention. See Bigham v. Godtfredsen, 857 F.2d 1415, 1417 (Fed. Cir. 1988). Section 112 provides, in relevant part:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The need of skilled artisans to experiment in order to "make and use" an invention does not preclude a finding of enablement under § 112, but that experimentation must not be "undue." In re Wands, 858 F.2d 731, 736-37 (Fed. Cir. 1988).

> Factors to be considered in determining whether a disclosure would require undue experimentation ... include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the

> relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Id. at 737. Enablement is a question of law. Id. at 735.

Having thoroughly analyzed the UK application, the Court finds that it complies with § 112 and thus enables skilled artisans to make and use the invention. The document describes the invention on its very first page as relating "to certain tetrahydrocarbazolone derivatives which may be used to promote gastric emptying and as anti-emetics." (UK Application at 1.) It then, using language identical to the '789 patent specification, identifies the compounds as "potent and selective antagonists" of the 5-HT_3 receptor. (Id. at 2.) The UK application also states: "[T]he invention provides [a formula of compounds] for use in the promotion of gastric emptying and for use as anti-emetics." (Id.) It provides a preferred compound for the invention, namely, ondansetron, and further offers specific dosages within a sufficiently narrow range. See Glaxo Group Ltd. v. Teva Pharm. Indus., Ltd., No. 02-219, 2004 U.S. Dist. LEXIS 16750, at *45-46 (D. Del. Aug. 20, 2004). Additionally, the UK application offers the following disclosure specifically addressing ondansetron's impact on nausea:

> Results from patients suffering from the symptoms of nausea indicate that the compounds of formula (1) alleviate the symptoms of nausea. The compounds may therefore also be of use as anti-emetics, i.e., in the prevention and treatment of nausea and vomiting.

(UK application at 6.)[3] Consequently, the Court concludes that skilled artisans would not need to

[3]While the Court acknowledges that the allegedly inconclusive West German studies were, at least in large part, the basis of this assertion, it does not deem this fact particularly relevant to the enablement argument here. In the § 112 enablement context, specification descriptions must be accepted as true unless there is reason to doubt the objective truth of those descriptions. In re Brana, 51 F.3d 1560, 1566 (Fed. Cir. 1995) (internal quotes and citation omitted). As the Court discusses in its inequitable conduct analysis below, no such reason existed during the relevant time period.

conduct undue experimentation in order to practice the invention. The UK application is sufficiently enabling.

The Court recognizes that the District of Delaware, in Teva, arrived at the same conclusion concerning enablement. See 2004 U.S. Dist. LEXIS 16750, at *41-49. As Teva was construing the same documents at issue here, that is, the UK application, the '789 patent, and the '628 patent, and because enablement is a legal question, Wands, 858 F.2d at 735, the Court adopts Teva.

Defendant contends that Teva was wrongly decided. Specifically, defendant argues that Teva failed to apply the Wands factors, and that it never properly construed the claims, rendering it impossible in any event to apply the Wands factors correctly to the full scope of TYERS I and II. (See, e.g., Def.'s Opp. Br. at 28-29.)

With respect to the first criticism, defendant is simply incorrect. Teva did set forth the relevant factors under Wands and applied at least three of these – namely, the quantity of experimentation necessary, the amount of guidance presented in the priority document, and the breadth of the claims – to the documents before it. See Teva, 2004 U.S. Dist. LEXIS 16750, at *43-46.

Defendant's entire argument is really thus rooted in the second criticism, which in essence rests on a claim construction yielding what plaintiffs aptly describe as a "universal" anti-emetic. Were the Court to read TYERS I and II as claiming a cure-all for nausea and emesis, defendant's arguments with respect to many of the Wands factors would gain strength. For example, the breadth-of-claims consideration, the final factor enumerated in Wands, 858 F.2d at 737, would arguably weigh heavily against plaintiffs, as a claim of a universal anti-emetic would

(especially in light of the fact that it does not, to this day, exist) require considerably more experimentation than a claim of an effective antagonist of a particular receptor. The Court, however, has rejected the sweeping construction sought by defendant. As a result, the UK application need only "give[] ample guidance to enable a person of ordinary skill in the art to administer ondansetron to treat emesis." Teva, 2004 U.S. Dist. LEXIS 16750, at *49. As discussed above, it does just that. See also id. (summarizing the reasons for the priority document's compliance with § 112).

For these reasons, defendant's motion for summary judgment of non-enablement is DENIED and plaintiffs' motion for summary judgment of enablement is GRANTED.

IV. *Inequitable Conduct*

Both parties have moved for summary judgment on the issue of inequitable conduct before the PTO. The Court finds that no reasonable fact-finder could conclude that there is clear and convincing evidence that plaintiff failed to disclose material information with an intent to mislead the PTO. See Bristol-Myers Squibb Co. v. Rhone-Poulenc Rorer, Inc., 326 F.3d 1226, 1233-34 (Fed. Cir. 2003).

In support of its own motion, and in opposition to plaintiffs' motion, defendant marshals the following evidence of inequitable conduct:

(a) plaintiffs' failure to disclose to the PTO the nature and results of the West German study described in the UK application, notwithstanding the assertion in that application that "[r]esults from patients suffering from the symptoms of nausea indicate that the compounds of formula (1) alleviate the symptoms of nausea"; and

(b) plaintiffs' statement in a brief submitted to the PTO during the Interference that

"[t]here was no reason to believe [in 1985] that a substance that was effective in the treatment of nausea and vomiting induced by one cause would not be effective in the treatment of nausea and vomiting induced by another cause."[4]

With respect to the plaintiffs' representations concerning the West German study, defendant's arguments are devoid of merit.

First, the study did in fact yield the results claimed by plaintiff in the UK application. (See Glaxo Group Research Ltd., A Pilot Study to Evaluate GR38032 in the Treatment of Migraine, Aug. 1985, at 2, 6.) The clinicians observed ondansetron's effect on the symptoms of migraine, including nauseau and vomiting, and that effect was positive. (Id. at 6.) Indeed, the study revealed that higher doses of the drug relieved the nausea or emesis of five of six patients. (Id. at 7.) Defendant attacks the statistical quality of the study, not its actual (and truthful) results. See Fiers v. Revel, 984 F.2d 1164, 1171-72 (Fed. Cir. 1993) (specification is presumptively truthful and party challenging enablement bears burden of impeaching its truthfulness); cf. Grefco, Inc. v. Kewanee Indus., Inc., 499 F. Supp. 844, 867-68 (D. Del. 1980) (finding inequitable conduct where patentee withheld unsuccessful tests and misrepresented results of disclosed tests). Consequently, a finding of actual intent to mislead is unsupportable as a matter of law.

Second, the record reveals that the West German study was merely the catalyst for the invention. The test results were analyzed against the backdrop of the art, particularly Dr. Gralla's studies with metoclopramide, a weak 5-HT_3 antagonist. (Tyers Dep. at 26:14-27-17.) Dr. Tyers'

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[4]Defendant does make various other arguments, but these arguments interrelate with the evidence the Court has just cited.

testimony in this regard is corroborated by Glaxo's investigative efforts that followed, which focused on chemotherapy-induced emesis. (See, e.g., Letter from Challoner to Smyth of 6/21/85.) When viewed in the context of the surrounding circumstances, instead of in a vacuum, plaintiffs' representations concerning the West German study appear anything but dishonest.

With respect to plaintiffs' representation during the Interference, that is, that "[t]here was no reason to believe [in 1985] that a substance that was effective in the treatment of nausea and vomiting induced by one cause would not be effective in the treatment of nausea and vomiting induced by another cause," defendant's arguments are likewise meritless.

First, the testimony of defendant's own expert, Dr. Hain, belies defendant's claim that this representation was "an outrageous lie." (Def.s' Moving Br. at 23.) Specifically, Dr. Hain testified that he "usually" administers Zofran® to "people with intractable nausea and vomiting of unknown cause." (Hain Dep. at 36:5-9.) Indeed, he stated that Zofran® actually worked for "maybe a quarter" of these people. (Id. at 37:18-38:7.) Dr. Hain further testified to administering, in the late 1970's, the anti-emetic Compazine for a wide variety of kinds of nausea, the causes of which all differed. (Id. at 94:1-97:12.) For this reason alone, defendant's charge is not only overwrought but directly contradicted by facts.

Second, and perhaps more important, it is not as if the PTO swallowed whole plaintiffs' supposed lie, relying solely on the alleged misrepresentation to resolve the contested issue of fact. To the contrary, Beecham made these same arguments during the Interference, presented evidence in support, and lost. (See, e.g., Reply Br. of the Party Wootton, at 7-8, 15.)

It bears noting that, as with its enablement argument, defendant is relying on a sweeping claim construction that would render any number of statements or omissions before the PTO

technically misleading. For example, defendant argues that, in light of the limitless scope of the claimed invention, and the fact that plaintiffs failed to reveal ondansetron's inability to relieve, say, motion sickness, plaintiffs engaged in inequitable conduct to satisfy § 112 by omitting information concerning ondansetron's comparatively limited potential as a drug. (See Def.'s Moving Br. at 26-27.) Again, the Court has not adopted such a claim construction, and defendant's arguments in this respect therefore fail.

In sum, there is no genuine triable issue concerning the existence of a necessary element of an inequitable conduct finding, namely, dishonesty in fact. See Bristol-Myers, 326 F.3d at 1233-34. Therefore, defendant's motion is DENIED and plaintiffs' motion is GRANTED.

V. *Infringement*

The only remaining issue is that of infringement. The infringement analysis involves two steps: first, the Court construes the claims; second, the Court "compares the accused [product] to the properly construed claims to determine whether each and every limitation of a claim is present, either literally or equivalently, in the accused [product]." Tate Access Floors, Inc. v. Interface Architectural Res., Inc., 279 F.3d 1357, 1365 (Fed. Cir. 2002).

In light of the claim construction set forth above, it cannot be gainsaid that defendant's product is infringing. It is an act of infringement "to submit ... an [ANDA] for a drug claimed in a patent or the use of which is claimed in a patent." 35 U.S.C. § 271(e)(2)(A). Defendant has submitted an ANDA for a generic version of ondansetron to treat nausea and vomiting. (See, e.g., Kali Labs., Inc., Application to Market a New Drug, Biologic, or an Antibiotic Drug for Human Use, Sept. 30, 2002, at 1 ("ANDA").) Defendant's drug specifically targets nausea and

vomiting associated with chemotherapy (e.g., cisplatin) and radiotherapy, as well as post-operative nausea. (ANDA, Kali's Draft Package Insert, at 01-081.) The ANDA moreover reveals that Zofran® and defendant's product are structurally identical. (ANDA, Side-by-Side Comparison of Package Inserts, at 01-124.)

Accordingly, it is clear that defendant's product, as described in the ANDA, is directed to "a method of treatment for the relief of nausea and vomiting which comprises administering to a human or animal subject in need thereof an effective amount for treatment for the relief of nausea and vomiting of [ondansetron]," thereby infringing claim 1 of both TYERS I and II. It is also clear that, because defendant's drug will be administered to treat chemotherapy-induced nausea, post-operative nausea, and the like, it also infringes the dependent claims at issue. For these reasons, plaintiffs' motion for summary judgment of infringement is GRANTED. Defendant's ANDA filing infringes claims 1, 4, 6, 8, 10, 12, 13 and 16 of the '789 patent, and claims 1 and 2 of the '628 patent.

CONCLUSION

For the reasons set forth above, defendant's motion for a claim construction is GRANTED, defendant's motion for summary judgment that plaintiffs are not entitled to their foreign priority date is DENIED, and defendant's motion for summary judgment of invalidity on the basis of plaintiffs' inequitable conduct is DENIED. Plaintiffs' motion for summary judgment that the priority document complies with the written description and enablement requirements of 35 U.S.C. § 112 is GRANTED, plaintiffs' motion for summary judgment of no inequitable conduct is GRANTED, and plaintiffs' motion for summary judgment of infringement is GRANTED. An appropriate order accompanies this Opinion.

DATED: July 26, 2005

/s/ Jose L. Linares
United States District Judge